Office Action Summary	Application No.	Applicant(s)	
	09/577,505	FRUDAKIS ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above claim(s) *4-16 and 21-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,17-20 and 62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-3, 17-20 and SEQ ID NO:307 and 308) in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-62 are pending.

Claim 62 has been added.

Claims 1-3 and 17-20 have been amended.

Claims 1-3, 17-20 and 62are examined on the merits.

Applicants added another claim, designated as claim 61 in Amendment A (Paper number 7). However, claim 61 was already pending in the instant application. The original numbering of the claims must be preserved throughout the prosecution. Misnumbered claim 61 in the said amendment has been renumbered 62 consistent with rule 37 CFR 1.126.

Priority

3. Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. The Examiner has noted that the instant application claims priority to the continuation-in-part of 09/534,825, filed March 23, 2000, which is a continuation-in-part of

09/289,198, filed April 9, 1999, which is a continuation-in-part of 09/062,451, filed April 17, 1998, which is a continuation-in-part of 08/991,789, filed December 11, 1997, which is a continuation-in-part of 08/838,762, filed April 9, 1997. The limitations of SEQ. ID. NO: 307 (800 base pairs) and SEQ ID NO: 308 (102 amino acids) are not disclosed in continuation-in-part applications '451, '789 or '762. However, both sequences are disclosed in continuation-in-part applications '825 and '198. Accordingly, examined claims 1-3 and 17-20 will be granted the priority date of April 9, 1998 corresponding to U.S. serial number 09/298,198.

Information Disclosure Statement

4. The information disclosure statement filed October 30, 2000 as Paper number 4 lists a number of documents that were to be considered by the Examiner. It is noted that Applicants have previously submitted documents on pages 1-5 to the PTO in prior applications. However, not all of the applications were available at the time of examination. Hence, the listed documents "lined through" were not reviewed during examination and not considered. Applicants are invited to submit the references for consideration.

Drawings

5. The drawings are objected to because of reasons cited on attached form PTO 948 completed by draftsman. Correction is required.

INFORMATION ON HOW TO EFFECT DRAWING CHANGES

6. **Correction of Informalities -- 37 CFR 1.85**

New corrected drawings must be filed with the changes incorporated therein. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings **MUST** be filed within the **THREE MONTH** shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

7. **Corrections other than Informalities Noted by Draftsperson on form PTO-948.**

All changes to the drawings, other than informalities noted by the Draftsperson, **MUST** be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings **MUST** be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections

Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.185(a). Failure to take corrective action within the set (or extended) period will result in **ABANDONMENT** of the application.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1, 2 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as

to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is broadly drawn to an isolated polypeptide comprising at least an immunogenic portion of a breast tumor protein encoded by a nucleotide sequence recited in SEQ ID NO: 307. Claims 17-20 are drawn to compositions that include the said polypeptide and/or an immunogenic portion of a breast tumor protein. Thus, all cited claims are broadly drawn to a genus of nucleic acid molecules that encompass a larger nucleic acid that contains portions of nucleic acid that encode the amino acid sequences of SEQ ID NO: 308 protein or an immunogenic portion of a breast tumor protein. The specification describes only the cDNA sequences of SEQ ID NO: 307. The specification does not describe any of the structural elements of a gene that would encode these actual DNA sequences of promoter and regulatory regions and introns, all defining elements of a "gene". The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polynucleotides encoding the claimed

polypeptides and variants thereof. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description, however, of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides encompassed and no identifying characteristic or property of the instant polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the 5' and 3' regulatory regions and untranslated regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the gene. Therefore, the structure of these elements is not conventional in the art and those skilled in the art would therefore not recognize from the disclosure that applicant was in possession of the genus of nucleic acid, including genes, comprising SEQ ID NO: 307 or fragments thereof.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of specific nucleotide sequences and the ability to screen, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as

broadly claimed. Applicant is referred to the revised interim guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Likewise, the specification does not contain any disclosure of the function of a full-length open reading frame (ORF) that includes SEQ ID NO: 307. The genus of cDNAs including SEQ ID NO: 307 are very large and members of the genus are variable because of the potentiality of the many different proteins they may encode. Therefore, many structurally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

10. Claim 62 is rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claim 62 is broadly drawn to "[a]n isolated polypeptide comprising an amino acid sequence having at least 90% identity to SEQ ID NO:308". The specification while being enabling for the polypeptide having the amino acid sequence of SEQ ID NO:308, does not reasonably provide enablement for variants that have at least 90% sequence identity. There is no guidance as to how to make these divergent sequences. The

products of these 90% sequence identical molecules may possess function that is not commensurate with the functions of the native protein. The 90% sequence identical amino acids may not maintain the activities proposed in the specification. It would seem that specific function(s) would be required to make the encoded protein useful for the applications disclosed in the specification, such as pharmaceutical compositions. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge of and guidance with regard to which amino acid or acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which the protein's structure relates to its function. The specification provides essentially no guidance as to which of the infinite possible choices is likely to be successful. The true fact of the state of the art in peptide chemistry is expressed succinctly in the accompanying Lazar article (Molecular and Cellular Biology 8(3): 1247-1252, March 1988). This article presents data that substantiates the fact that the introduction of mutations in an amino acid sequence will yield products with different biological activity from the wild type protein.

From the discussion above, it is clear that the predictability of changes to the amino acid sequence is practically nil as far as biological activities are concerned. The specification fails to provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed nucleic acids in a manner reasonably correlated with the broad scope of the claims. Without such guidance, the changes which must be made

in the nucleic acid sequence of SEQ ID NO: 307, which results in nucleic acid sequences with 90% identity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

11. Claims 1, 2 and 17-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 broadly is drawn to a polypeptide comprising at least an immunogenic portion of a breast tumor protein. These portions are to be contained in compositions that invoke an immunogenic response as presented in claims 17-20. However, all portions of the breast tumor protein cannot be deemed immunogenic. It is not clear if any portion of the breast tumor protein can be used for instance to induce a variety of cytokines that affect general host responses. The specification has not presented evidence of the use of an immunogenic portion of a breast tumor protein, nor has the specification clearly distinguished how one of ordinary skill in the art could identify the presence of a unique, highly antigenic protein or how to use them. There is a dearth of extensive chemical characterization of the structure of this breast tumor protein. This is in fact necessitated in order to elucidate its effectiveness as an immunogenic portion capable of establishing an immunogenic response. The attached review authored by Walter (Journal of Immunological Methods 88:149-161, 1986) discusses the selection of potential antigenic determinants and the considerations required to identify potential

immunogens. An effective immune response (i.e. generation of antibodies) is dependent upon criteria suggested by Walter. Undoubtedly, there needs to be a correlation between for instance the conformation, the hydrophilicity and the size of the alleged immunogenic portion.

The specification suggests the use of immunogenic portions of the breast tumor in compositions that would establish an immunogenic response, however clinically successful specific cancer immunotherapy depends on the identification of the immunogenic portions or tumor-rejection antigens. Applicants have not defined what amino acid residues are clearly immunogenic, nor presented objective evidence that supports the use of these portions in assays, for example that analyze either T-cell or antibody responses of cancer patients against autologous cancer cells or define predicted immunogenic epitopes. It is not clear that any immunogenic portion of Applicants' breast tumor protein would even generate a modest immune response or how to generate relatively potent immune responses. Hence, there is lack of instruction in the specification enabling one skilled in the art to make and practice the invention commensurate within the scope of the claim utilizing immunogenic portions of a breast tumor protein. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art. For the above reasons, it appears that undue experimentation would be required to use the claimed invention.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "under moderately stringent conditions" in claim 1 is not clear. The specification on page 14, lines 12-20 does set forth one example of these conditions, however one of skill in the art could not be apprised of the full scope which is not limited by the claim. The metes and bounds of the claimed polynucleotides are unclear, in absence of limitations specifying specific stringency conditions.

Double Patenting

14. Claims 1-3 and 17-20 directed to an invention not patentably distinct from claim 1-3 and 17-20 of commonly assigned U.S. Application 09/534,825 (filed March 23, 2000). Specifically, the instant application claims an isolated polypeptide, SEQ ID NO:308 comprising at least an immunogenic portion of a protein, wherein the protein is encoded by a polynucleotide sequence, SEQ ID NO:307 (claims 1-3). Claims 17-20 are drawn to compositions containing the claimed polypeptide.

The claims of the instant application and U.S. Application 09/534,825 differ because the '825 application not only claims polypeptide, SEQ ID NO: 308 and the nucleic acid (SEQ ID NO: 307) that encodes it, but additional sequences comprised in a pharmaceutical composition and vaccine. Specifically, claims 1-3 of U.S. Application 09/534,825 are drawn to a number of isolated polypeptides, including SEQ ID: 308, which is encoded by SEQ ID NO: 307. Claims 17-20 of this application are drawn to

compositions containing polypeptides, including amino acids designated as SEQ ID NO:308. The breadth of these claims encompasses the subject matter claimed in the instant application.

15. The U.S. Patent and Trademark Office normally will not institute interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Application 09/534,825, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225

USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-3 and 17-20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 and 17-20 of copending Application No. 09/534,825 (filed March 23, 2000). Although the conflicting claims are not identical, they are not patentably distinct from each other because both are drawn to an isolated polypeptide, SEQ ID NO:308 encoded by polynucleotide sequence, SEQ ID NO:307, as well as compositions comprising SEQ ID NO: 308.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 1-3, 17-20 and 62 are free of the art.

Conclusion

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is

(703) 306-5880. The examiner can normally be reached on 6:30 am to 4:00 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4315 for regular communications and (703) 308-4315 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Alana M. Harris, Ph.D.
February 25, 2002